REMARKS

First, Applicants wish to thank Examiners Zhou and Marschel for their time and helpful suggestions during their interview with Applicant's representative, Cheryl H. Agris on December 20, 2005. During the interview, the structure of the Appeal Brief, in particular, where to discuss why certain claims were designated separately patentable in Section VII. Additionally, there was a discussion regarding which rejections are still pending. The Examiner has issued an Advisory Action dated December 20, 2005. Applicants below respond to issues raised in the Advisory Action.

1. **Rejection of Claims 1-19, 21-39, 41, 51 and 52 under 35 U.S.C. §112, First Paragraph (written description)**

Claims 1-19, 21-39, 41, 51 and 52 remain rejected under 35 U.S.C. §112, first paragraph. It is asserted that the amendment submitted on 7/19/04 would not overcome the rejection because new matter was introduced.

Applicants respectfully traverse the rejection. Arguments traversing the rejection were set forth in the accompanying Appeal Brief. However, in order to advance prosecution, claims 1-19, 21-38, 41, 51 and 52 have been canceled without prejudice.

Claim 39 has been amended to be rewritten in independent form and thus conforms with 37 C.F.R. §41.33(b). Amended claim 39 is directed to a method for inhibiting function of an RNA by contacting the RNA, under conditions permissive for hybridization, with a modified nucleotide compound which includes MN_3M, where N is a phosphodiester-linked unmodified 2'-deoxynucleoside moiety containing at least one guanine, adenine, cytosine or thymine moiety and M is a methylphosphonate-containing deoxynucleoside. Claim 39 is explicitly supported by the specification at page 8, lines 17-26:

> The invention also provides a method of inhibiting the function of an RNA, which method comprises contacting, under conditions permissive of hybridization, the RNA with a complementary modified nucleotide compound which includes at least one component selected from the group consisting of **MN_3M**, B(N)xM and M(N)xB wherein N is a phosphodiester-linked modified or unmodified 2'-deoxynucleoside moiety; M is a moiety that confers endonuclease resistance on the nucleotide component and contans at lest one modified or unmodified nucleic acid base; B is a moiety that confers exonuclease resistance to the terminus to which it is attached; and x is an integer of at least 2.

Further support can be found in original claim 39. Thus, amended claim 39 does not contain new matter.

In view of the above arguments and arguments set forth in the accompanying Appeal Brief, the cancellation of claims 1-19, 21-38, 41, 51 and 52 and the amendment of claim 39, Applicants assert that the rejection of claims 1-19, 21-39, 41, 51 and 52 have been overcome. Therefore, Applicants respectfully request that the rejection be withdrawn.

2. The Rejection of Claims 1-2, 4 8 12-14, 19 and 42-50 Under 35 USC §102(b)

Claims 1-2, 4, 8, 12-14, 19 and 42-50 have been rejected under 35 U.S.C. §102(b) as being anticipated by Miller et al. It is asserted that the product disclosed by Miller et al. is the same as the claimed product since the Miller et al. product would act as an RNase H substrate when complexed with a complementary RNA.

Before discussing the rejection, Applicants note that in order to advance prosecution, claims 1-2, 4, 8, 12-14, 19 and 42-43, 45-48 and 50 have been

canceled. Claims 44 and 49 have been amended to be rewritten in independent form and thus conforms with 37 C.F.R. §41.33(b). Amended claim 44 recites that the claimed compound acts as an RNase H substrate when complexed with complementary RNA and that each nuclease resistant component comprises at least one moiety which confers endonuclease resistance and at least one moiety which confers exonuclease resistance and that 2 or more contiguous phosphodiester-linked 2' deoxynucleosides are located between the moiety conferring endonuclease resistance and the moiety conferring exonuclease resistance. Amended claim 49 contains the further limitation that the compound additionally contains a modified oligonucleotide or polynucleotide, which consists of at least one moiety which confers endonuclease resistance and at least one moiety which confers exonuclease reisstance.

Applicants respectfully traverse the rejection. Appellants point out that anticipation requires that the claimed invention to have been known in the prior art "in the detail of the claim" such that each element and limitation contained in the claim is present in a single prior art reference, "arranged as in the claim". *Karsten Mfg. Corp. v. Cleveland Golf CO.* 242 F.3d 1376, 58 USPQ2d 1286 (Fed. Cir. 2001). Clearly, Miller et al., 1985 does not contain each and every element of the subject matter claimed.

Appellants note that the sequences disclosed in Miller et al., 1985 either completely contain methylphosphonate linkages or just a 5'-phosphodiester unmodified moiety (see Figure 3 of Miller et al., 1985). None of the compounds disclosed in Miller et al., 1985 contain **two separate** nuclease resistant components.

Appellants further note that the cited Miller et al. reference is silent with respect to the RNase H sensitivity of the methylphosphonate sequences disclosed in Figure 3. However, it is most likely that these sequences are RNase H resistant. For example, Cazenave et al., 1989, Nucl. Acids Res.

17:4255-4273 (**Tab 2** and cited in the instant application) discloses that a methyl phosphonate 17-mer "failed to induce the degradation of the target mRNA by the E. coli RNase H". Additionally, Furdon et al., 1989, Nucl. Acids Res. 17:9193-9204 (**Tab 3**) discloses results from studies with a 14-mer oligonucleotide containing one to six methylphosphonate linkages. Results from the Furdon et al. studies indicated that "Susceptibility to cleavage by RNase H increased parallel to a reduction in the number of methylphosphonate residues in the oligonucleotide"[1]. It is further noted in Furdon et al., 1989, Nucl. Acids Res. 17:9193-9204[2]

> RNA hybridized to MP-oligos containing one or two methylphosphonate deoxynucleosides was cleaved by RNase H almost a easily as that in the control duplex with D-oligo,,,,RNA in duplexes with MP-oligos which contained three, four and six methylphosphonate deoxynucleosides, i.e., in which methylphosphonate bonds were separated by three, two or one phosphodiester bond...was increasingly resistant to cleavage by the enzyme.

In view of the above arguments and amendments, Applicant assert that the rejection under 35 U.S.C. §102(b) has been overcome. Therefore, Applicants respectfully request that the rejection be withdrawn.

3. Conclusion

Appellants assert that these claim amendments put the claims in condition for allowance or at least obviate some issues on appeal.

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[1] See abstract in Furdon et al., 1989, Nucl. Acids Res. 17:9193-9204
[2] See Furdon et al. at page 9202

If a telephone conversation would further the prosecution fo the present application, Applicants' undersigned attorney request that he be contacted at the number provided below.

Respectfully submitted,

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